

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 22 November 1999 (22.11.99)	
International application No. PCT/EP99/01966	Applicant's or agent's file reference PG3376/PCT
International filing date (day/month/year) 24 March 1999 (24.03.99)	Priority date (day/month/year) 26 March 1998 (26.03.98)
Applicant MARRIOTT, Christopher et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

07 October 1999 (07.10.99)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer F. Baechler Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

CRAWLEY, Karen
Glaxo Wellcome plc
Glaxo Wellcome House
Berkeley Avenue
Greenford
Middlesex UB6 0NN
ROYAUME-UNI

Date of mailing (day/month/year) 13 September 2000 (13.09.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference PG3376/PCT	
International application No. PCT/EP99/01966	International filing date (day/month/year) 24 March 1999 (24.03.99)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input checked="" type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address MARTIN, Gary, Peter King's College London Manresa Road London SW3 6LX United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input checked="" type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence
Name and Address MARTIN, Gary, Peter King's College London Franklin-Wilkins Building London SE18WA United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Athina Nickitas-Etienne
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

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1. The following indications appeared on record concerning:

☒ the applicant ☒ the inventor ☐ the agent ☐ the common representative

Name and Address MARRIOTT, Christopher King's College London Manresa Road London SW3 6LX United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
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	Teleprinter No.	

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Name and Address MARRIOTT, Christopher King's College London Franklin-Wilkins Building London SE18WA United Kingdom	State of Nationality GB	State of Residence GB
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<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Athina Nickitas-Etienne Telephone No.: (41-22) 338.83.38
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Date of mailing (day/month/year) 13 September 2000 (13.09.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference PG3376/PCT	
International application No. PCT/EP99/01966	International filing date (day/month/year) 24 March 1999 (24.03.99)

1. The following indications appeared on record concerning:

☒

the applicant

☒

the inventor

☐

the agent

☐

the common representative

Name and Address

ZENG, Xian, Ming
King's College London
Manresa Road
London SW3 6LX
United Kingdom

State of Nationality

CN

State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐

the person

☐

the name

☒

the address

☐

the nationality

☐

the residence

Name and Address

ZENG, Xian, Ming
King's College London
Franklin-Wilkins Building
London SE18WA
United Kingdom

State of Nationality

CN

State of Residence

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the receiving Office

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the International Searching Authority

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the International Preliminary Examining Authority

☐

the designated Offices concerned

☒

the elected Offices concerned

☐

other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Athina Nickitas-Etienne

Telephone No.: (41-22) 338.83.38

PCT INTERNATIONAL COOPERATION TREATY

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From the INTERNATIONAL BUREAU

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Glaxo Wellcome plc
Glaxo Wellcome House
Berkeley Avenue
Greenford
Middlesex UB6 0NN
ROYAUME-UNI

Date of mailing (day/month/year)

03 November 2000 (03.11.00)

Applicant's or agent's file reference

PG3376/PCT

IMPORTANT NOTIFICATION

International application No.

PCT/EP99/01966

International filing date (day/month/year)

24 March 1999 (24.03.99)

1. The following indications appeared on record concerning:

☒

the applicant

☒

the inventor

☐

the agent

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the common representative

Name and Address

ZENG, Xian, Ming
King's College London
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United Kingdom

State of Nationality

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Name and Address

ZENG, Xian, Ming
14 Newburgh Road
Rectory Gardens
Grays, Essex RM17 6UG
United Kingdom

State of Nationality

CN

State of Residence

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Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒

the receiving Office

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the International Searching Authority

☒

the elected Offices concerned

☒

the International Preliminary Examining Authority

☐

other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Athina Nickitas-Etienne

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

21 JUL 2000

WIPO

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PG3376/pct	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP99/01966	International filing date (day/month/year) 24/03/1999	Priority date (day/month/year) 26/03/1998
International Patent Classification (IPC) or national classification and IPC A61K9/00		
Applicant GLAXO GROUP LIMITED		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 07/10/1999	Date of completion of this report 19.07.2000
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Stoltner, A Telephone No. +49 89 2399 8408 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/01966

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-28 as originally filed

Claims, No.:

1-18 as originally filed

Drawings, sheets:

1/3-3/3 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/01966

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1-18
	No:	Claims
Inventive step (IS)	Yes:	Claims 1-18
	No:	Claims
Industrial applicability (IA)	Yes:	Claims 1-18
	No:	Claims

2. Citations and explanations

see separate sheet

ad section V:

- 1). The present application concerns a process for manufacturing crystals with particular characteristics such as controlled surface-smoothness, size, shape and degree of crystallinity. Said crystals with a particularly well defined morphology results find use in the manufacture of pharmaceutical inhaled formulations exhibiting advantageous properties. Said crystals are manufactured by a crystallisation process as depicted under steps (a)-(e) in claim 1.
- 2). With respect to the present subject-matter the following documents have been researched and considered:
 - D1, WO-A-9 505 805, relates to a process for providing a stable crystalline form of a fine-grained substance, comprising lactose and active ingredients such as salbutamol or ipratropium (cf. abstract and page 6, lines 16-31 and page 7, lines 4-36). On page 4, lines 23-36 and page 5, lines 1-14, D1 describes the process of how to obtain such stable crystals. D1, however, does nowhere refer to a crystallisation method whereby the viscosity of the crystallisation medium is adjusted as presently depicted.
 - D2, WO-A-9 623 485, concerns the method of producing a powder for use in dry powder inhalers (cf. page 24, last line bridging with page 25, lines 1-14). Said powder includes active particles (cf. page 18, lines 15-18) and carrier particles (lactose) for carrying the active particles and further includes also additive material (a glidant) which is attached to the surfaces of the carrier particles in order to promote the release of the hereto attached active particles. D2, however, is silent on a crystallisation process as presently claimed and compositions containing such crystals.
 - D3, WO-A-9 638 153, provides amorphous stable solid dispersions of misoprostol, using excipients like carbopol in an amorphous state and lactose in crystalline form (cf. page 3, "Summary of the invention", lines 1-26, page 4, lines 12-34, and page 5, first line).

- D4, International Journal of Pharmaceutics, 116(1), march 1995, pp. 113-118, G. Buckton et al., studies the use of isothermal microcalorimetry in the change of crystallinity of spray-dried salbutamol sulfate (cf. abstract). D4 shows that salbutamol sulfate recrystallizes in water vapour by a cooperative process and compares salbutamol recrystallization with data for the recrystallization of spray-dried lactose. There is however, no reference to a crystallization process as presently depicted.
- 3). A crystallization process as defined in steps (a)-(e) of claim 1 is nowhere disclosed nor suggested in the cited documents. As consequence the skilled man in art would by no means be led to the crystals resulting from said process and to the inhaler formulations manufactured by way of said process. In the light of the above cited documents the subject-matter of the present set of claims has to be recognised both novel and inventive pursuant to Arts. 33(2) and 33(3) PCT.

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PG3376/pct	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 99/ 01966	International filing date (day/month/year) 24/03/1999	(Earliest) Priority Date (day/month/year) 26/03/1998
Applicant GLAXO GROUP LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

IMPROVED CRYSTAL STRUCTURE

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 9/00, 9/12, 31/135	A1	(11) International Publication Number: WO 99/48475 (43) International Publication Date: 30 September 1999 (30.09.99)
(21) International Application Number: PCT/EP99/01966 (22) International Filing Date: 24 March 1999 (24.03.99) (30) Priority Data: 9806477.7 26 March 1998 (26.03.98) GB (71) Applicant (for all designated States except US): GLAXO GROUP LIMITED [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): MARRIOTT, Christopher [GB/GB]; King's College London, Manresa Road, London SW3 6LX (GB). MARTIN, Gary, Peter [GB/GB]; King's College London, Manresa Road, London SW3 6LX (GB). ZENG, Xian, Ming [CN/GB]; King's College London, Manresa Road, London SW3 6LX (GB). (74) Agent: CRAWLEY, Karen; Glaxo Wellcome plc, Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: IMPROVED CRYSTAL STRUCTURE (57) Abstract A process for the production of crystals with controlled surface smoothness, size, shape and degree of crystallinity, compositions comprising such crystals, and the use of certain crystals, especially lactose, lactose monohydrate, fluticasone propionate, salmeterol xinafoate, salbutamol sulphate or ipratropium bromide in pharmaceutical compositions.		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
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BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
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CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/01966

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K9/00 A61K9/12 A61K31/135

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 95 05805 A (ASTRA AB ;BRIGGNER LARS ERIK (SE); TROFAST EVA ANN CHRISTIN (SE)) 2 March 1995 (1995-03-02) *cf. abstract, page 1,1st para., page 4, lines 23-38 bridging with page 5, lines 1-14, page 6, lines 21-31 and page 7, lines 4-15*	1-18
Y	WO 96 23485 A (CO ORDINATED DRUG DEV ;STANIFORTH JOHN NICHOLAS (GB)) 8 August 1996 (1996-08-08) *cf. abstract, page 4, lines 9-26, page 24, last line bridging with page 25, lines 1-14, claims*	1-18
	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

30 July 1999

Date of mailing of the international search report

17/08/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Stoltner, A

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/01966

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 96 38153 A (SEARLE & CO ;KARARLI TUGRUL T (US); OTTO DAVID (US); PENZOTTI STAN) 5 December 1996 (1996-12-05) *cf. abstract and page 3, "summary of the invention", lines 1-26, page 4, lines 12-34 and page 5, first line*</p> <p>---</p>	1-18
A	<p>G. BUCKTON ET AL.: "The use of isothermal microcalorimetry in the study of changes in crystallinity of spray-dried salbutamol sulfate" INTERNATIONAL JOURNAL OF PHARMACEUTICS, vol. 116, no. 1, 14 March 1995 (1995-03-14), pages 113-118, XP002110839 *cf. abstract, page 116, left col., 2nd para. and right col., lines 1-12*</p> <p>-----</p>	1-18

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 99/01966

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9505805 A	02-03-1995	AU 681186 B	21-08-1997
		AU 7626494 A	21-03-1995
		BR 9407320 A	16-04-1996
		CN 1133004 A	09-10-1996
		CN 1195523 A	14-10-1998
		CZ 9600544 A	15-05-1996
		EP 0717616 A	26-06-1996
		FI 960869 A	26-02-1996
		HU 74000 A	28-10-1996
		JP 9501930 T	25-02-1997
		NO 960744 A	23-02-1996
		NZ 273090 A	24-06-1997
		PL 313142 A	10-06-1996
		SG 47760 A	17-04-1998
		SK 23496 A	05-02-1997
		US 5709884 A	20-01-1998
		US 5637620 A	10-06-1997
		US 5874063 A	23-02-1999
		ZA 9405675 A	29-04-1996
WO 9623485 A	08-08-1996	AU 699131 B	26-11-1998
		AU 4545696 A	21-08-1996
		BG 101858 A	30-04-1998
		BR 9607490 A	23-12-1997
		CA 2211874 A	08-08-1996
		CZ 9702443 A	14-01-1998
		EP 0806938 A	19-11-1997
		FI 973151 A	30-09-1997
		HU 9802209 A	01-02-1999
		JP 10513174 T	15-12-1998
		NO 973502 A	30-09-1997
		NZ 300654 A	25-02-1999
		PL 321572 A	08-12-1997
		SK 103697 A	14-01-1998
		ZA 9600721 A	19-08-1996
WO 9638153 A	05-12-1996	AU 5794196 A	18-12-1996
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